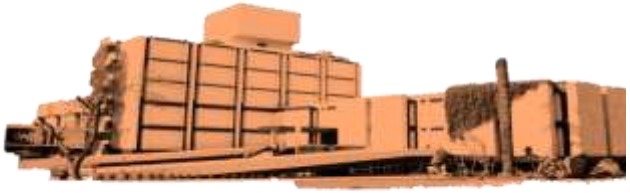


INCIDENCE AND STUDY OF SOME CHRONIC COMPLICATIONS OF DIABETES MELLITUS AFTER LIVE KIDNEY DONATION IN MANSOURA UROLOGY AND NEPHROLOGY CENTER (A RECORD BASED STUDY)

By

Mohammad Megahed Abu El Magd

Introduction and aim of the work

Introduction & Aim of the work

- **Renal transplantation is the golden method for management of end-stage renal disease and kidney transplant recipients have a higher quality of life and consume fewer health care resources compared with patients on dialysis.**

- **Living kidney donation has become an essential part of transplantation practice.**
  - **Shortage of deceased donors.**
  - **The growing waiting lists.**
  - **Tendency for pre-emptive transplantation.**

(Yoo et al., 2009) , (Fuggle et al., 2010).

Introduction & Aim of the work

- **Diabetes mellitus is the leading cause of end-stage renal disease.**
- **Diabetes mellitus is an absolute contraindication to living donation. Prospective donors with an increased risk of type 2 diabetes mellitus because of family history, ethnicity or obesity should undergo a glucose tolerance test and only be considered further as donors if this is normal.**

(Fehrman et al.,1996), (Bethesda., 2007).

INTRODUCTION & AIM OF THE WORK

- **This line of post-donation researches initiated in our center mainly aims to identify potential medical burdens of live kidney donation, design prevention protocols ,modify donor inclusion-exclusion criteria and finally to inform donors about the potential risks of donation.**
- **This research aim is to:-**

  1. Estimate the prevalence of diabetes mellitus after live kidney donation.

  2. Assess some risk factors for diabetes mellitus and their impact on developing the studied chronic complications after live kidney donation.

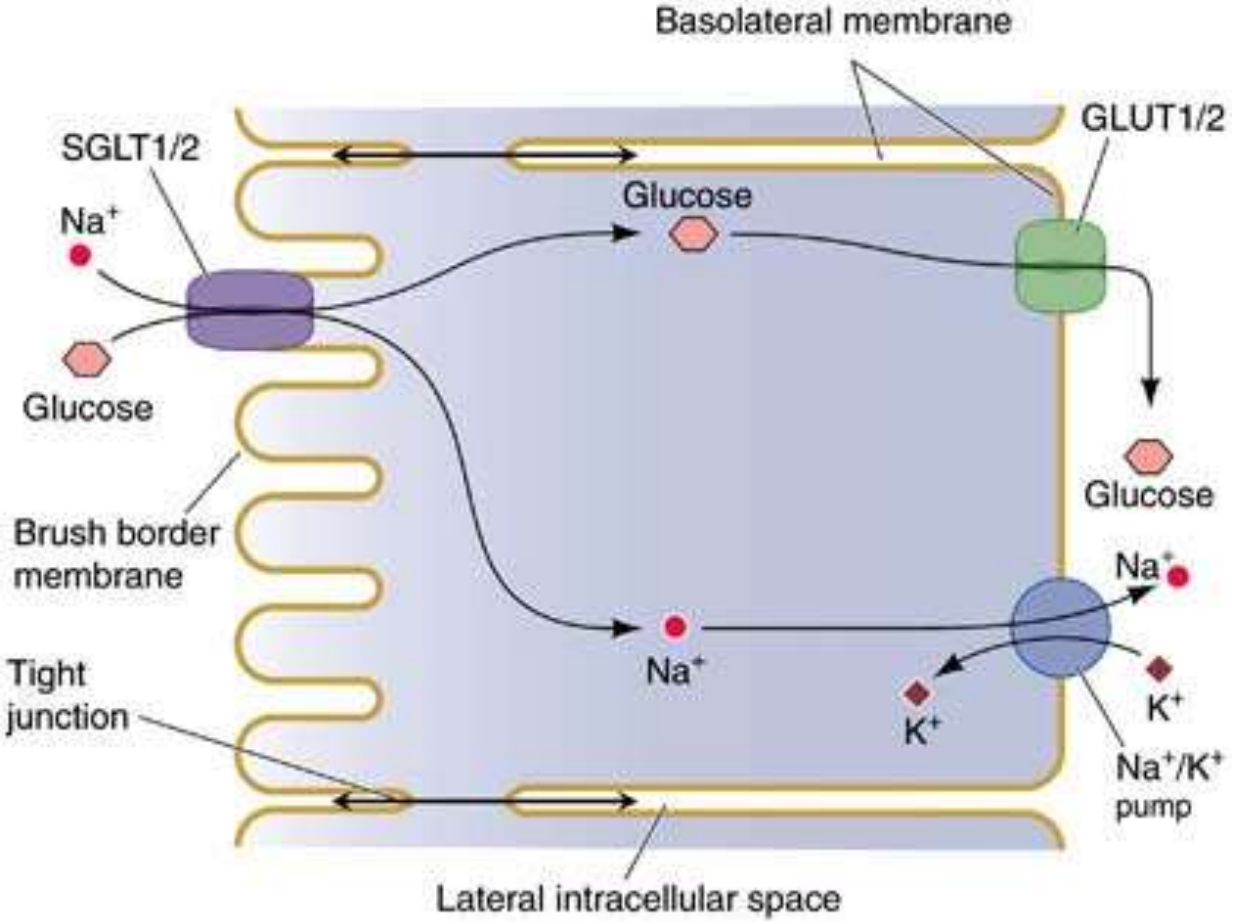
  3. Study some chronic complications of diabetes mellitus after live kidney donation.

(Fehrman et al.,1996), (Bethesda., 2007).

Review of literature

Review of literature

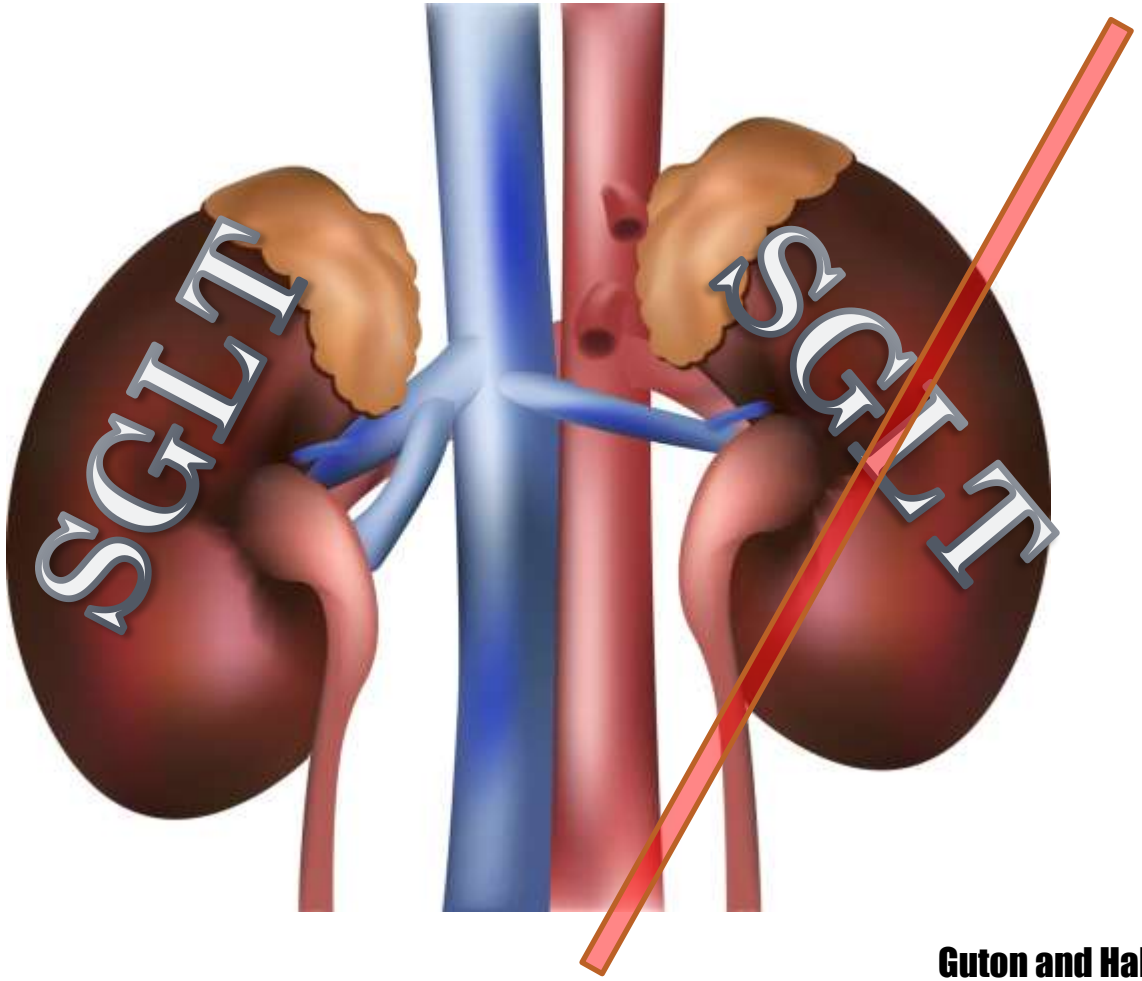
- **Role of kidney in glucose homeostasis**



Guton and Hall., 12th Edition

Review of literature

- **Role of kidney in glucose homeostasis**



Guton and Hall., 12th Edition

Renal Glucose Reabsorption in Type 2 Diabetes

WorldWIDE
Worldwide Initiative for Diabetes Education

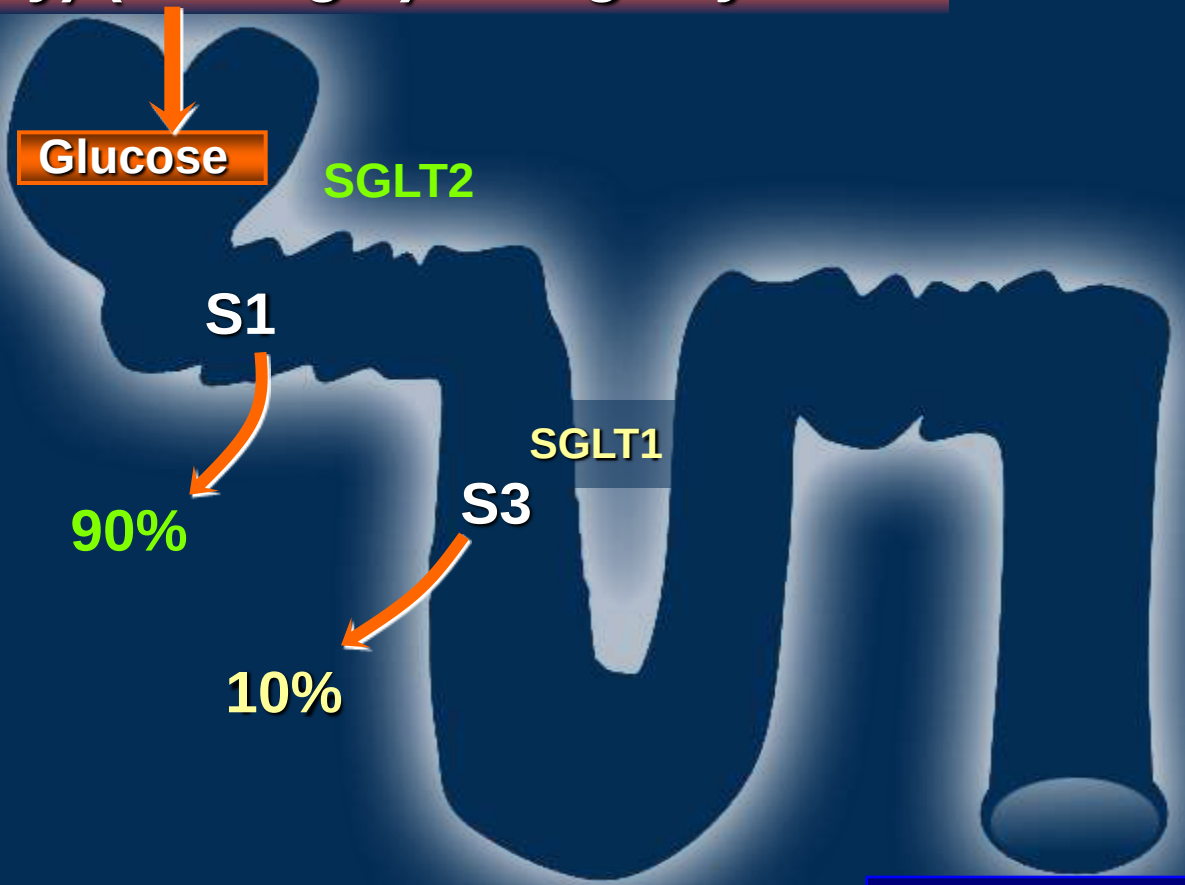
- Sodium glucose cotransporter 2 (SGLT2) plays a role in renal glucose reabsorption in proximal tubule
- Renal glucose reabsorption is increased in type 2 diabetes
- Selective inhibition of SGLT2 increases urinary glucose excretion, reducing blood glucose

Wright EM, et al. *J Intern Med*. 2007;261:32-43.

Renal Handling of Glucose

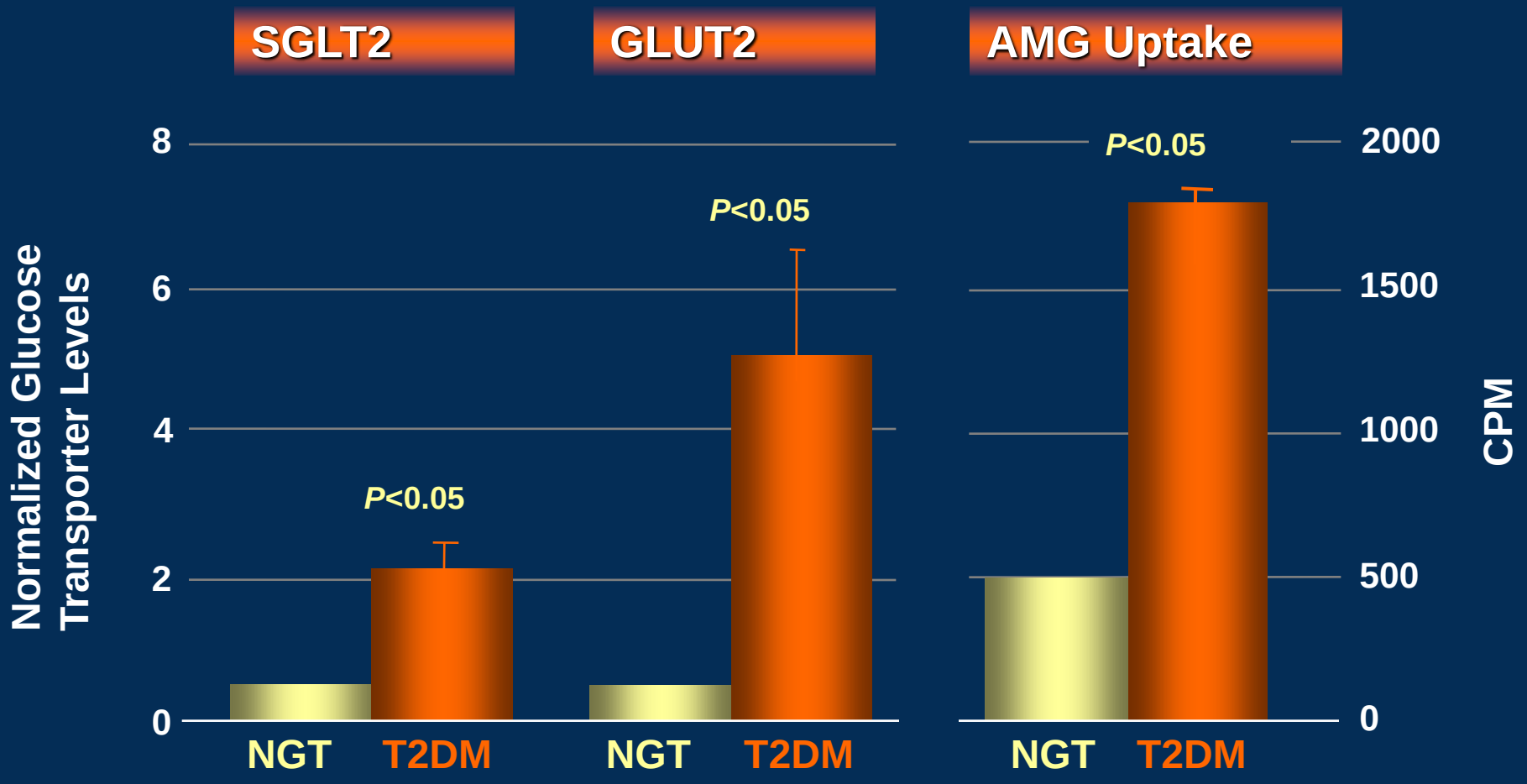
WorldWIDE
Worldwide Initiative for Diabetes Education

(180 L/day) (900 mg/L)=162 g/day



Increased Glucose Transporter Proteins and Activity in Type 2 Diabetes

WorldWIDE
Worldwide Initiative for Diabetes Education

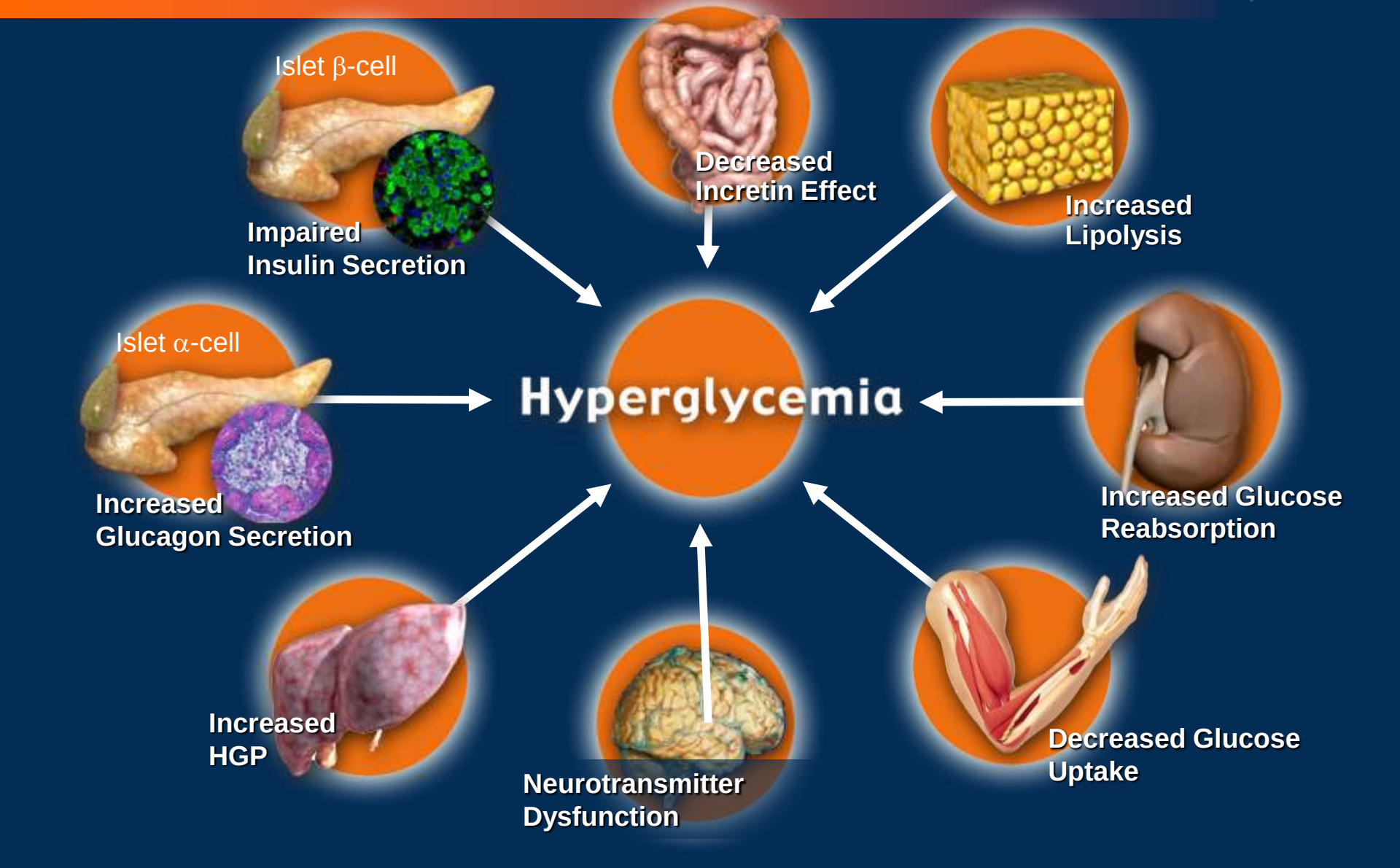


AMG=methyl-α-D-[$U^{14}C$]-glucopyranoside; CPM=counts per minute.

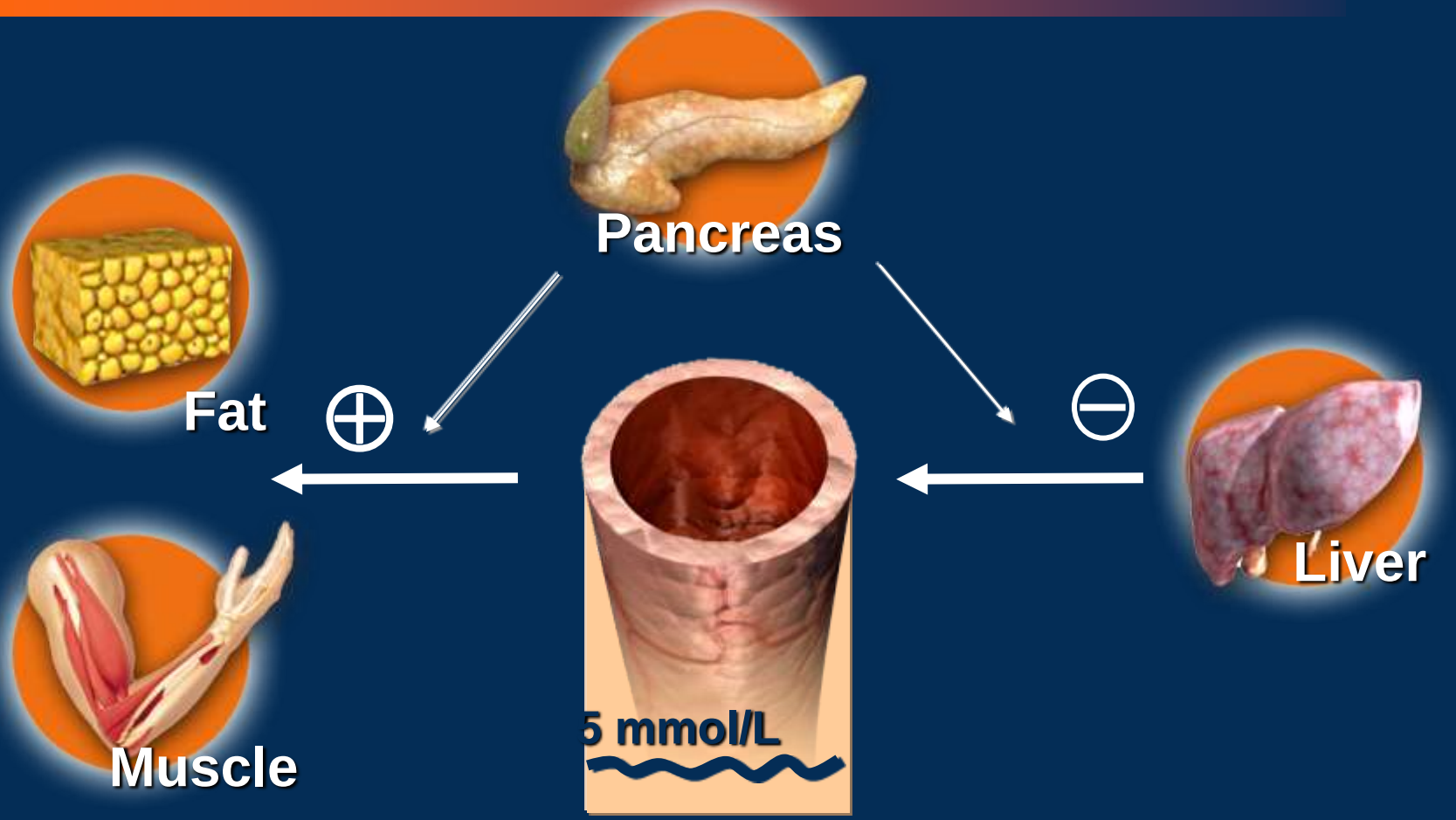
Rahmoune H, et al. *Diabetes.* 2005;54:3427-3434.

The Ominous Octet

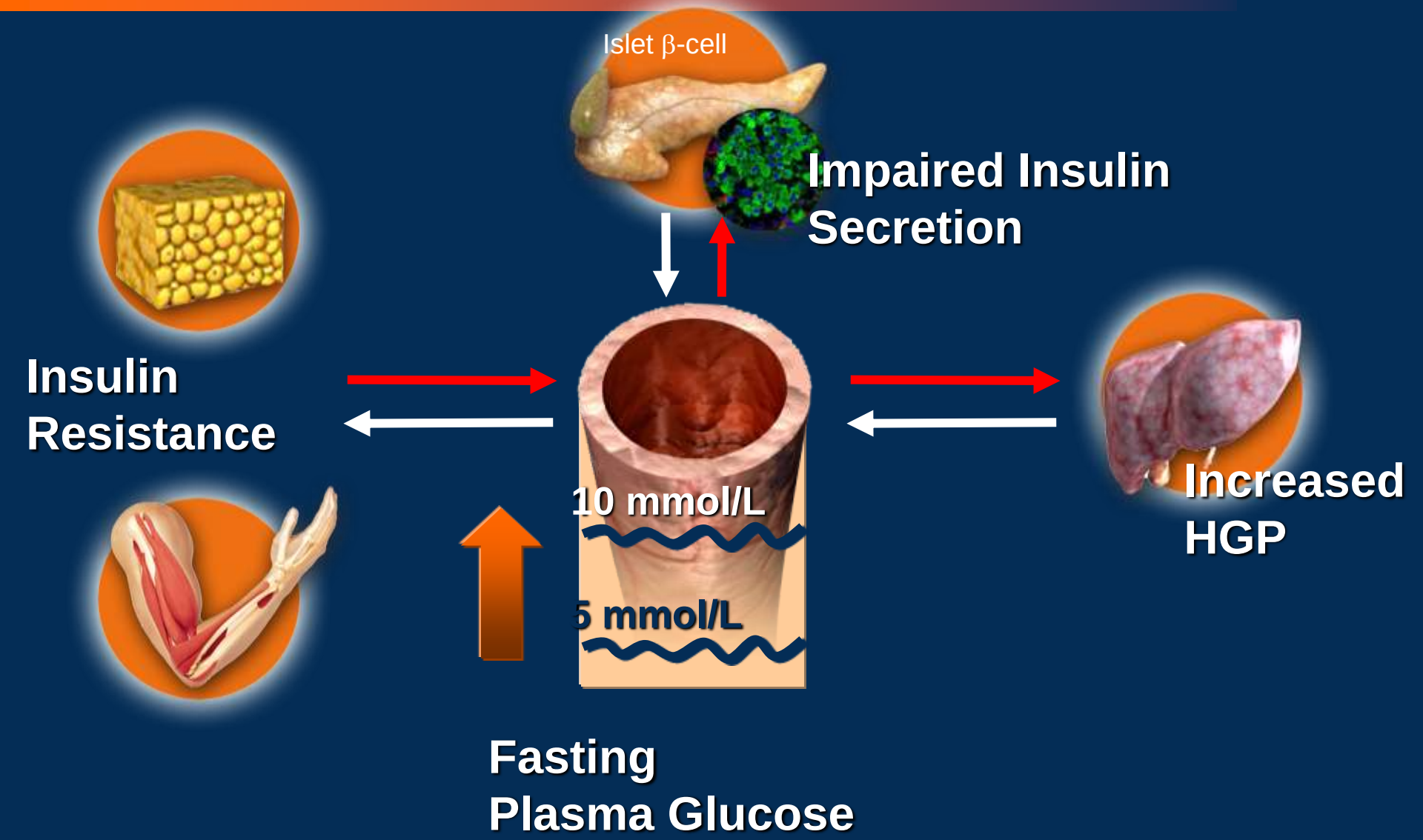
WorldWIDE
Worldwide Initiative for Diabetes Education



Normal Glucose Homeostasis



Pathophysiology of Type 2 Diabetes



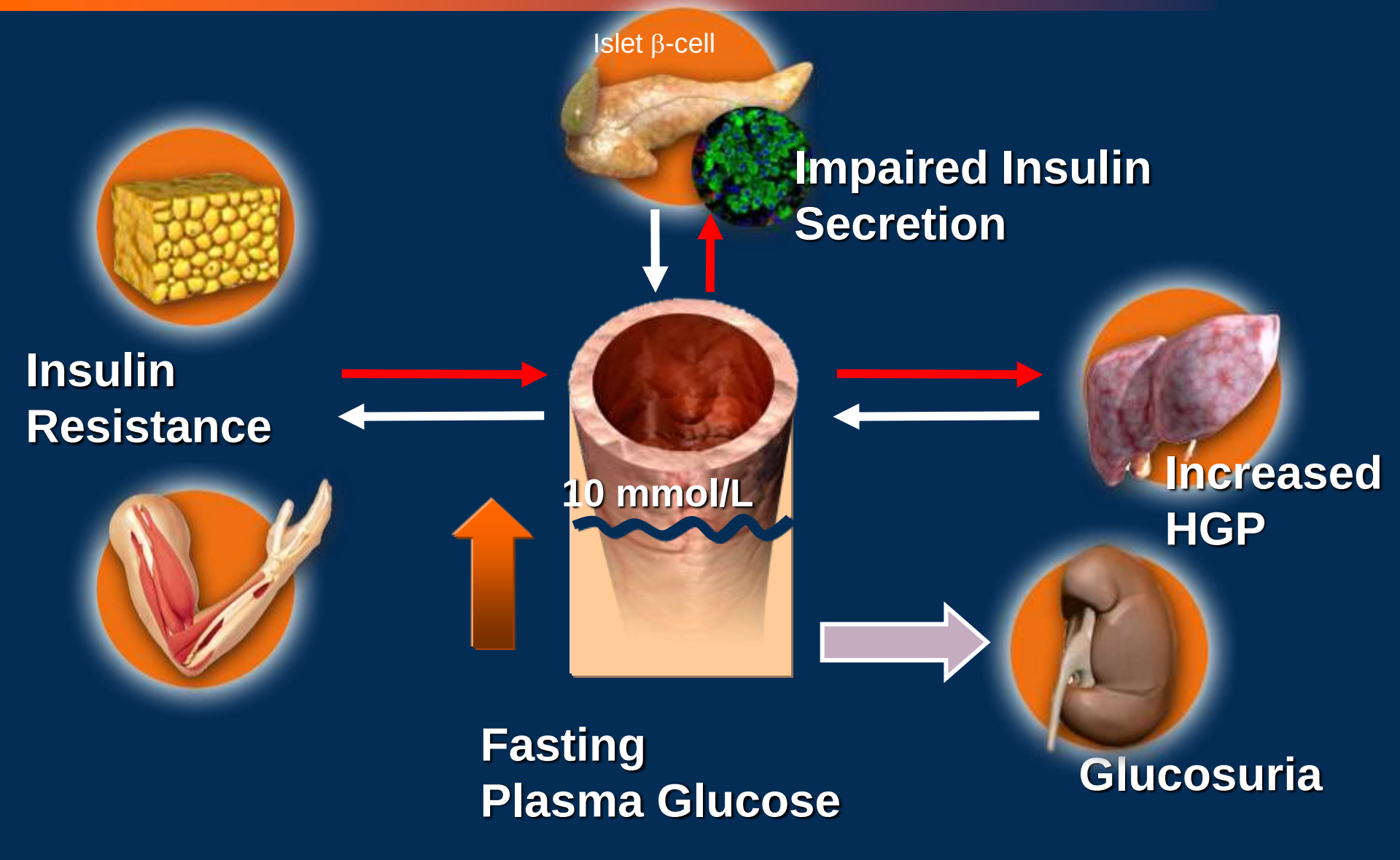
Rationale for SGLT2 Inhibitors

WorldWIDE
Worldwide Initiative for Diabetes Education

- Inhibit glucose reabsorption in the renal proximal tubule
- Resultant glucosuria leads to a decline in plasma glucose and reversal of glucotoxicity
- This therapy is simple and nonspecific
- Even patients with refractory type 2 diabetes are likely to respond

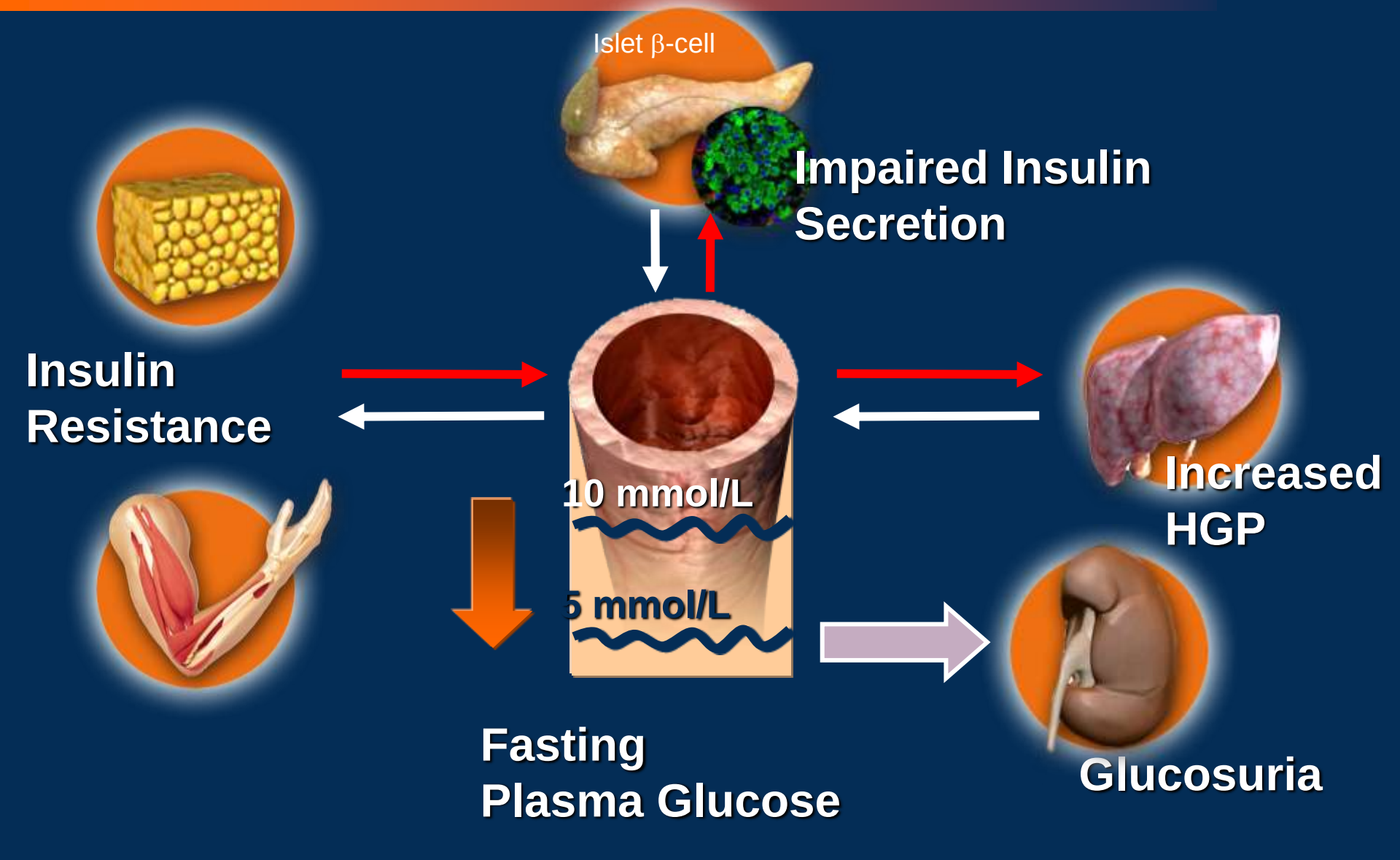
Pathophysiology of Type 2 Diabetes

WorldWIDE
Worldwide Initiative for Diabetes Education



Pathophysiology of Type 2 Diabetes

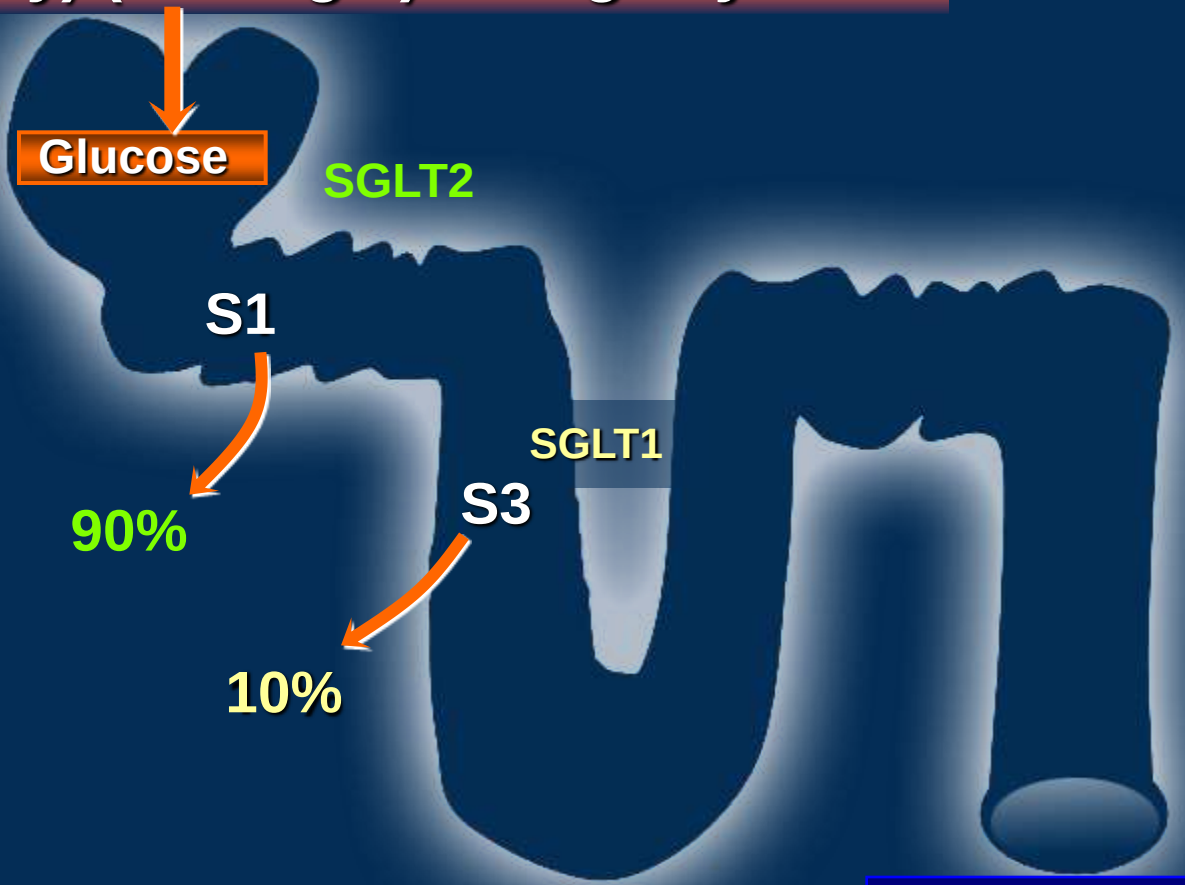
WorldWIDE
Worldwide Initiative for Diabetes Education



Renal Handling of Glucose

WorldWIDE
Worldwide Initiative for Diabetes Education

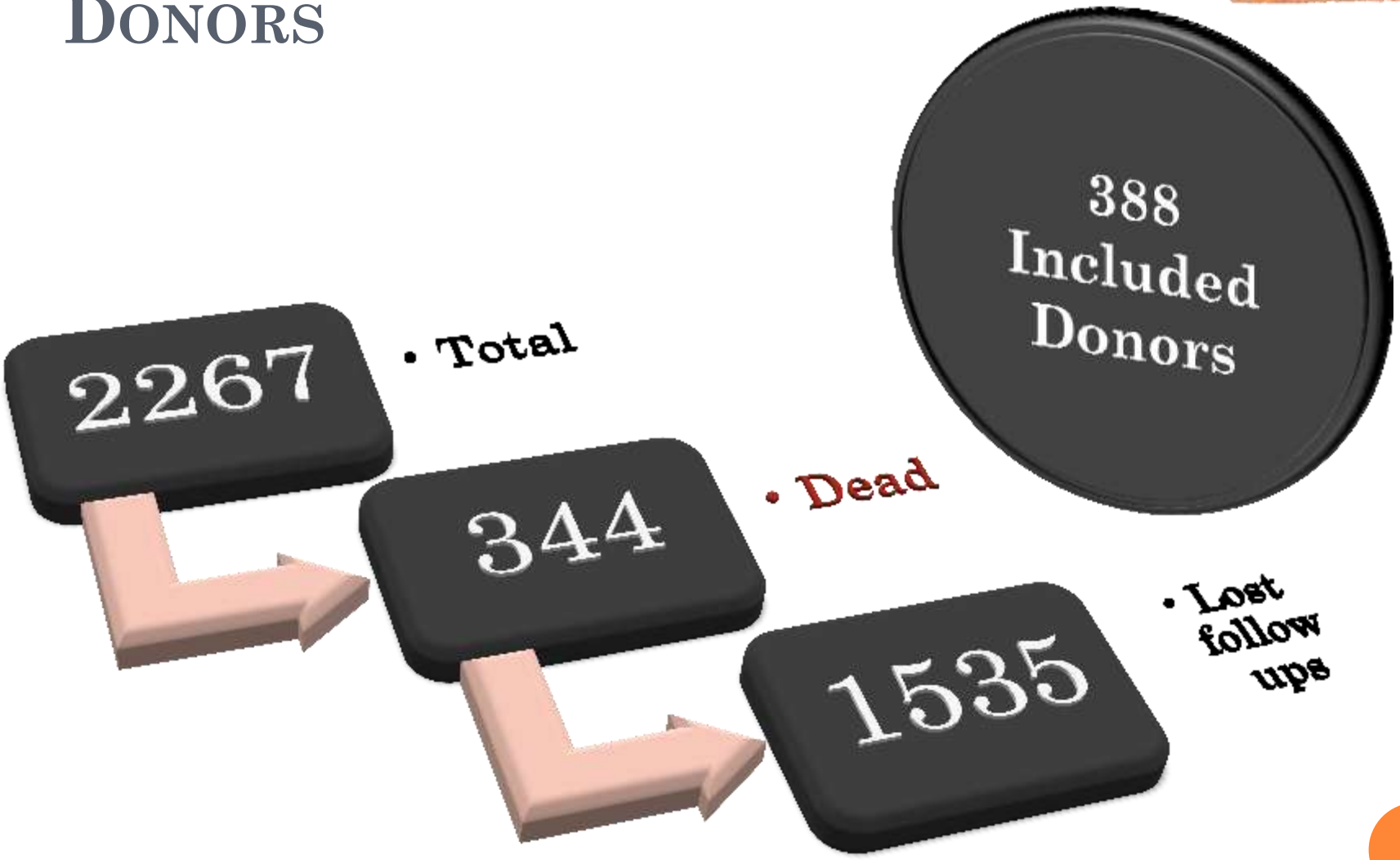
(180 L/day) (900 mg/L)=162 g/day



21st May 2014 UNC

Donors and Methods

Donors


388 Included Donors
2267
• Total
344
• Dead
1535
• Lost follow ups

METHODS

1. **Pre-Operative collected data:**
    1. Age at time of donation.
    2. Family history of diabetes mellitus.
    3. Body mass index (BMI) at the time of donation.
    4. Blood pressure at time of donation.
    5. Fasting and two hour post prandial blood glucose.
    6. Creatinine clearance by 24 hour urine collection method.
    7. Measurement of 24 hour urinary protein excretion.

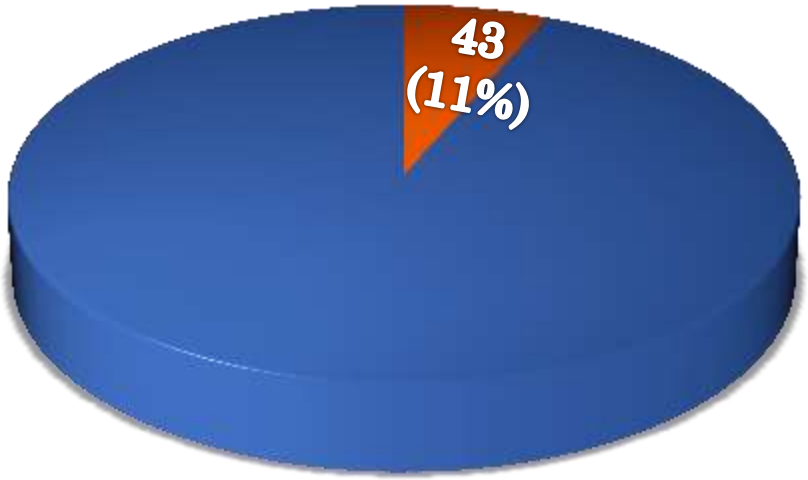
2. **Post-Operative collected data:**
    1. Serial monitoring of donors BMI.
    2. Serial Monitoring of blood pressure.
    3. Type of antihypertensive treatment if present.
    4. Serial measurement of Fasting blood sugar levels.
    5. Type of anti-hyperglycemic treatment.
    6. Serial monitoring of post-donation albumin creatinine ratio.
    7. Serial monitoring of estimated creatinine clearance by the application of the CKD-EPI equation.
    8. Serial monitoring of lipid profile post-donation.
    9. Fundus Examination for the diabetic donors only.

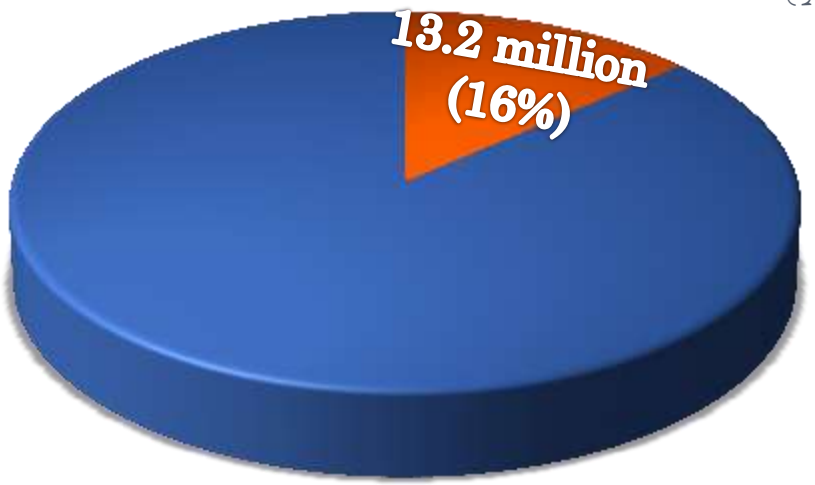
Results & Discussion

Results & Discussion

P 0.013

International Diabetes Federation
Atlas 2013





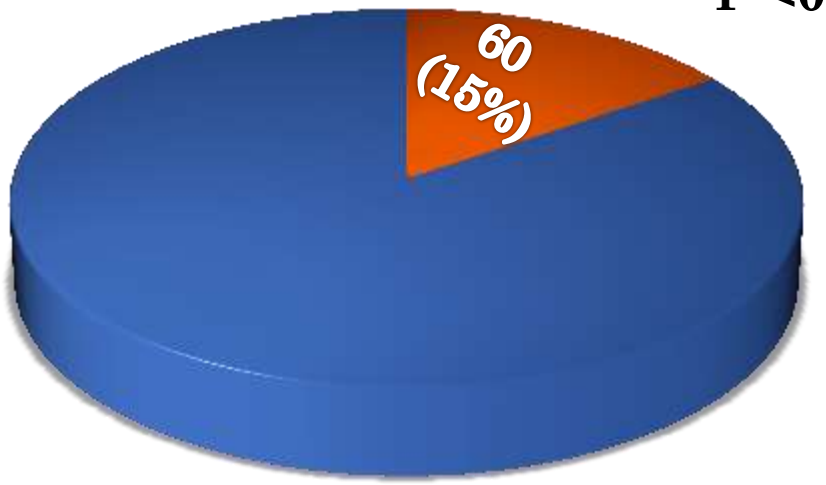
388 Studied Donors

85.25 million 2013 National Egyptian population

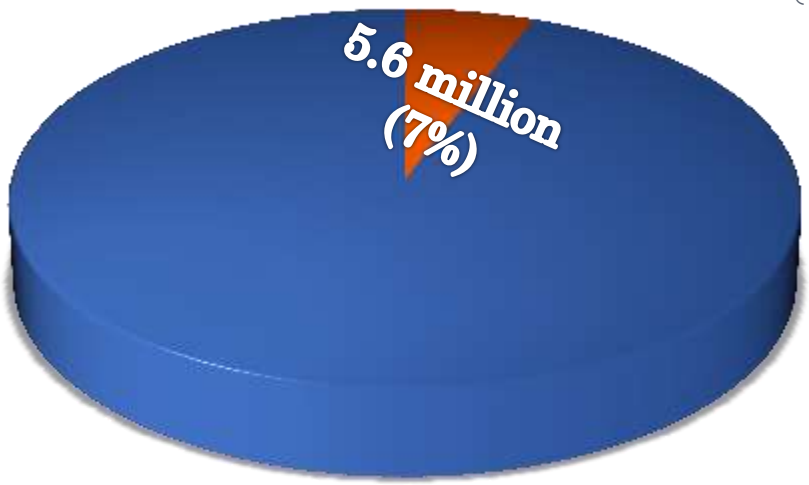
- **Diabetic Donors**
- **Diabetic Population**

Results & Discussion

P <0.0001



388 Studied Donors



85.25 million 2013 National Egyptian population

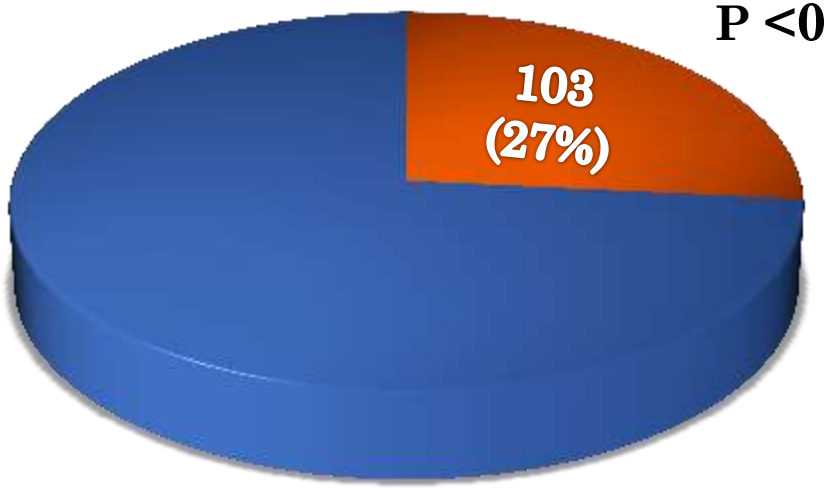
Prediabetic Donors

Prediabetic Population

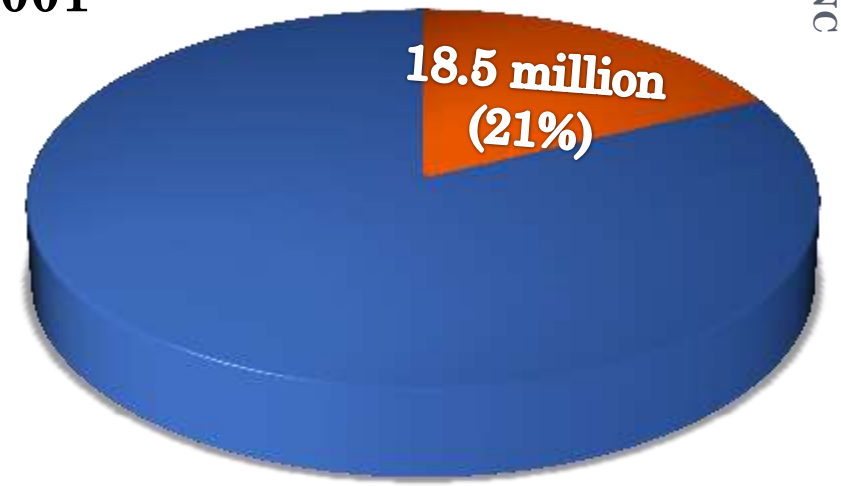
Results & Discussion

International Diabetes Federation Atlas 2013

P <0.0001



388 Studied Donors

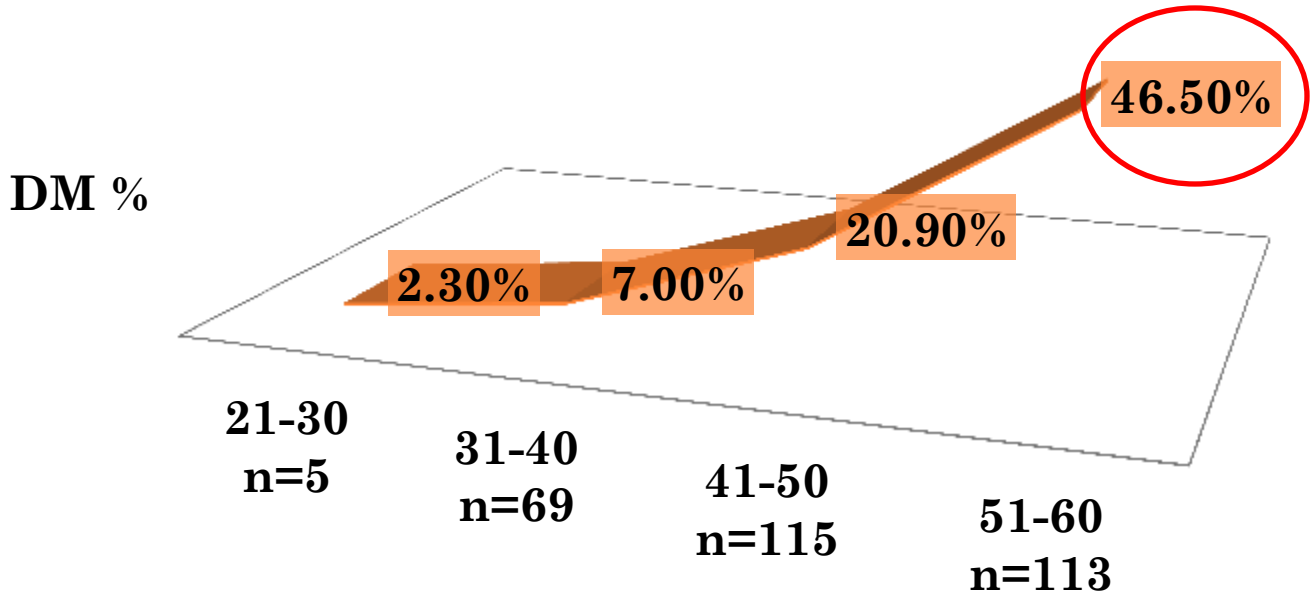


85.25 million 2013 National Egyptian population

- Disturbed glucose homeostasis Donors
- Disturbed glucose homeostasis Population

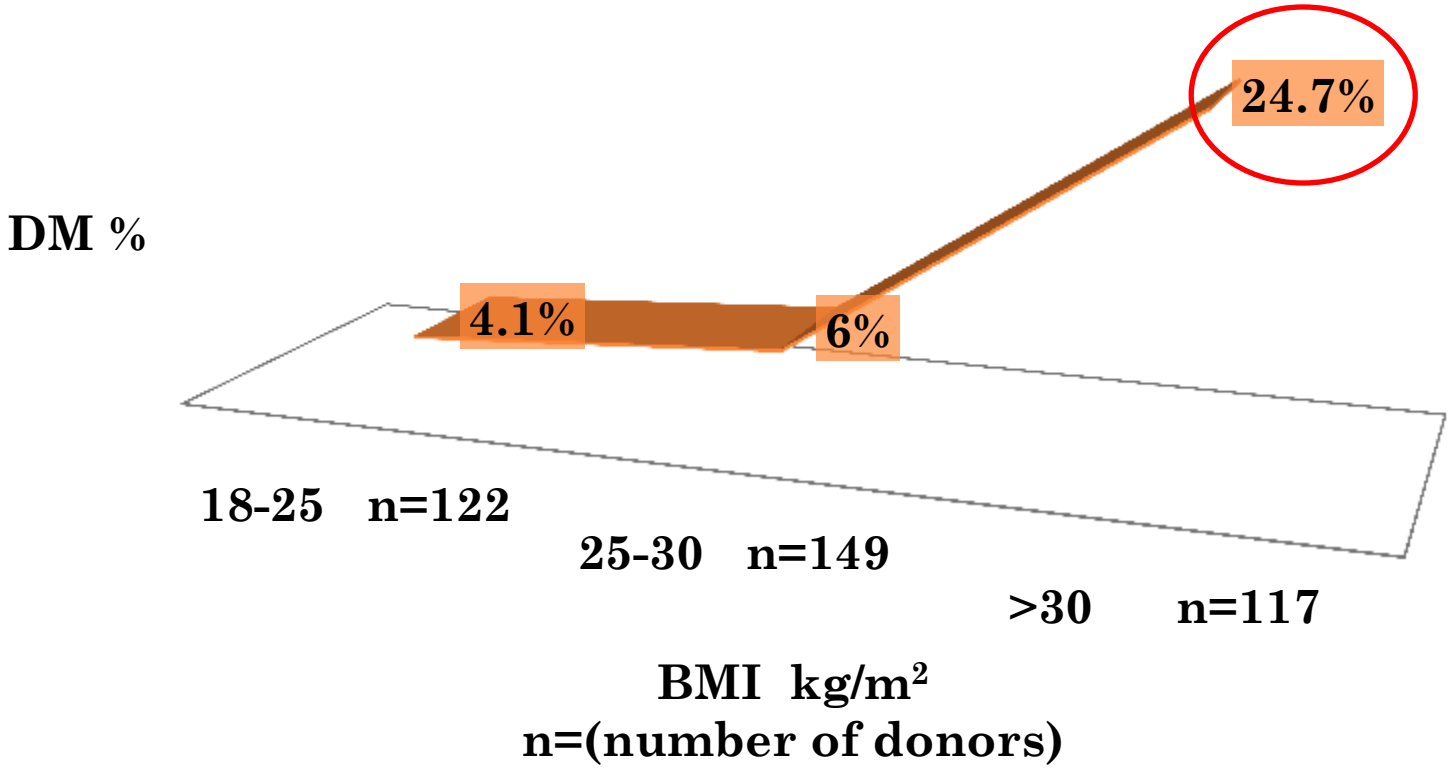
RESULTS & DISCUSSION

Percentage of DM among different donor age groups



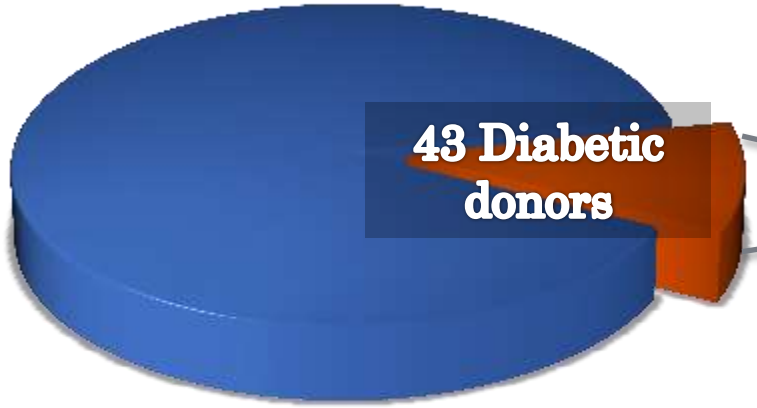
Results & Discussion

Percentage of DM among different donor BMI groups

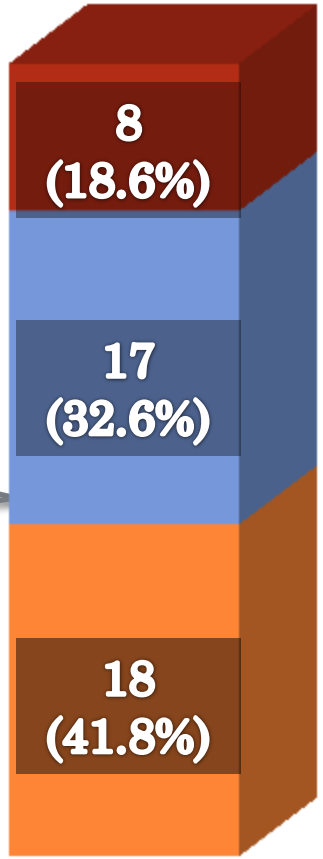


Results & Discussion

Percentage of microalbuminuric, macroalbuminuric and normoalbuminuric diabetic donors



388 Studied Donors



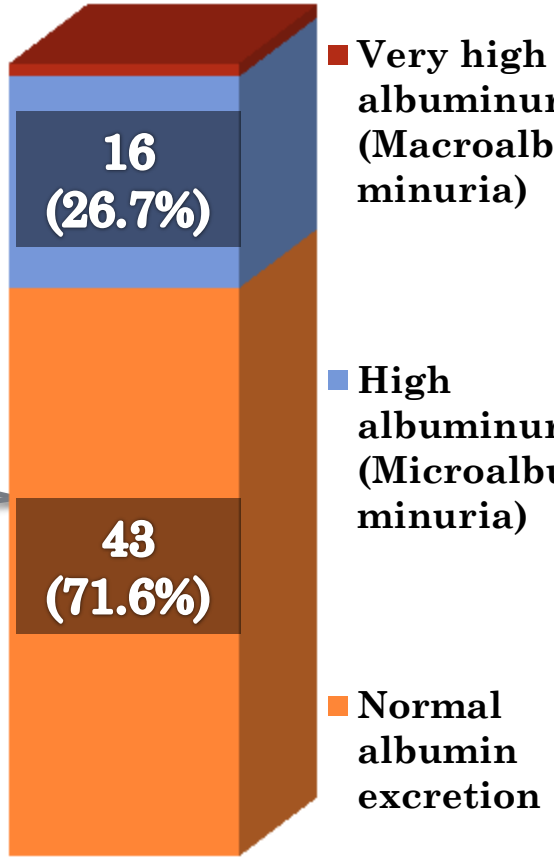
- Very high albuminuria (Macroalbu minuria)
- High albuminuria (Microalbu minuria)
- Normal albumin excretion

- Diabetic donors

Results & Discussion

Percentage of microalbuminuric, macroalbuminuric and normoalbuminuric prediabetic donors

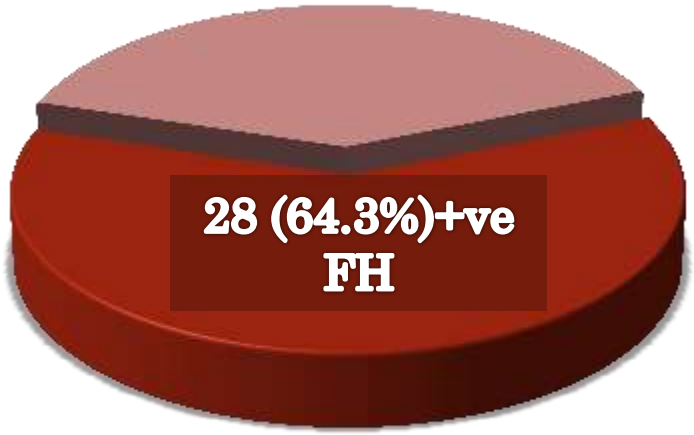
388 Studied Donors



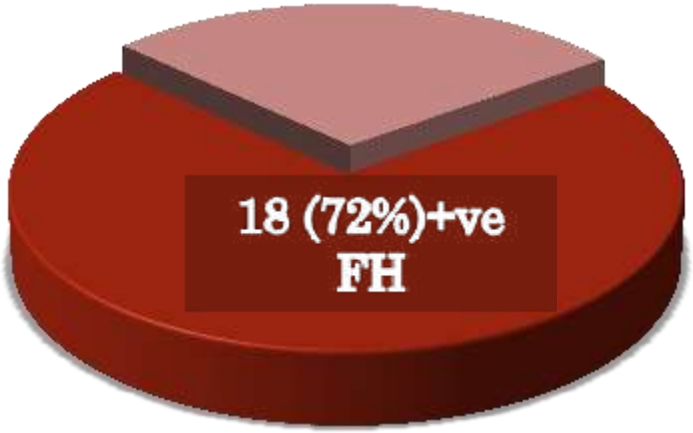
Prediabetic donors

Results & Discussion

Frequency of diabetes mellitus and high, very high albuminuria &or decreased eCrcl among diabetic donors with a family history of DM compared to diabetic donors with no family history of DM.



43 studied diabetic donors

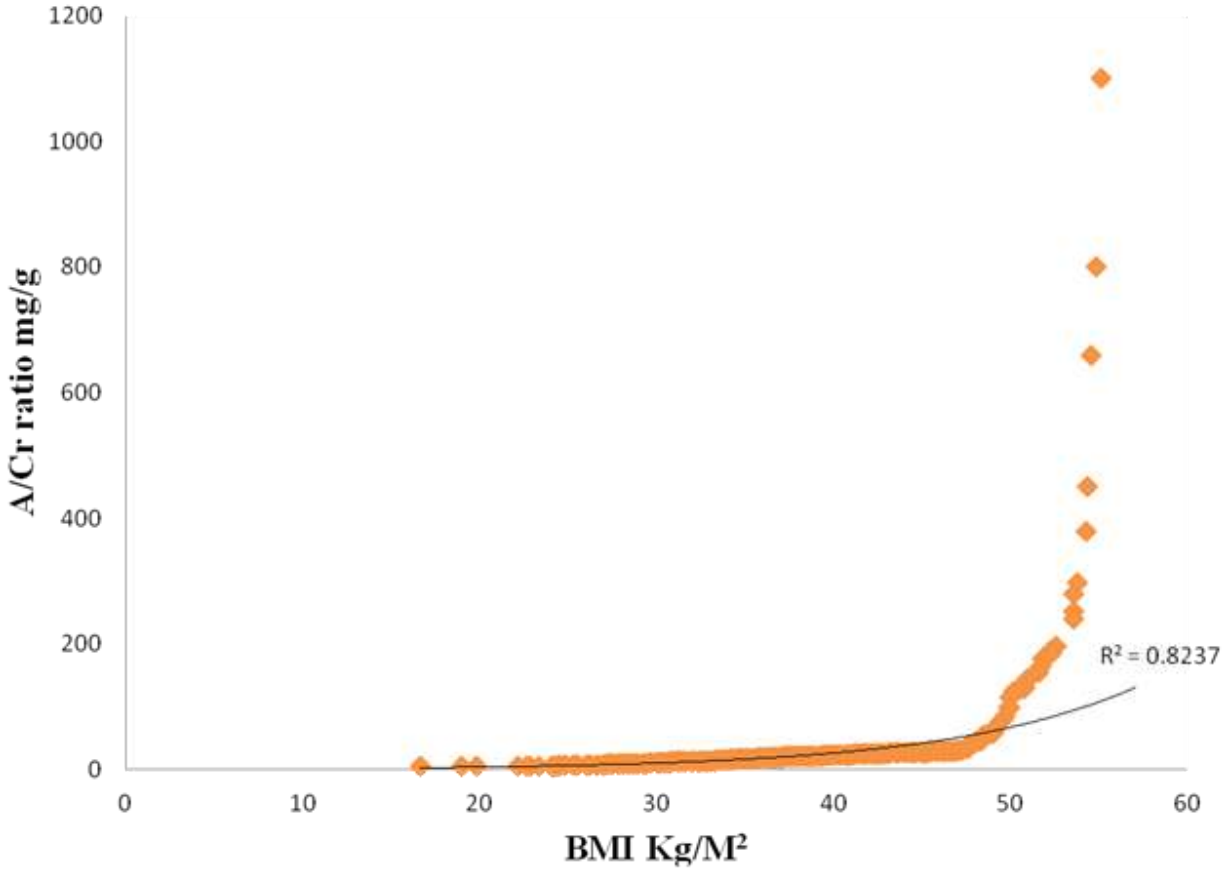


25 Donors with urinary ACR above 30 mg/g and or decreased Clearance below 70 ml/min

- **Diabetic donors with positive family history for DM**
- **Diabetic donors with high, very high albuminuria &or decreased Crcl and positive family history for DM**

Results & Discussion

- **Correlation between BMI and urinary albumin creatinine ratio in the whole studied group.**



Results & Discussion

Comparison between Diabetic Donors on RAS blockade versus Diabetic Donors on other or no antihypertensive drugs.

	On RAS blockade	Not on RAS blockade	P Value
Frequency, (%)	36/43 (83.7%)	7/43 (16.3%)	**< 0.0001**
Creatinine Clearance by CKD-EPI equation Ḿ ±SD (range) ,ml/min/1.37m^2	66.3 ±20.7 (35-122)	64.3±16.8 (31-84)	0.32
Urinary albumin creatinine Ratio median (range) , mg/g	96.5 (3-450)	1758.3 (118-6700)	**0.017**

Results & Discussion

Comparison between diabetic donors on insulin containing versus non-insulin containing regimens.

	Diabetic donors on insulin	Diabetic donors not on insulin	P Value
Frequency, (%)	14*/43 (32.6%)	29/43 (67.4%)	
Creatinine clearance by CKD-EPI equation Ḿ ±SD (range) ,ml/min/1.37m^2	68.2 ±16.9 (56-118)	67.2 ±23 (31-122)	0.44
Urinary albumin creatinine ratio Median (range) , mg/g	29 (11-40)	45 (3-6700)	**0.01**

*11 donors were on insulin plus (non-metformin) oral hypoglycemic drugs and 3 donors only were on insulin alone. No donors were on insulin + metformin.

Results & Discussion

Comparison between diabetic donors on metformin containing versus other oral hypoglycemic containing regimens.

	Diabetic donors on metformin containing regimens	Diabetic donors On other oral hypoglycemic agents	P Value
Frequency, (%)	25/43 (58.1%)	15*/43 (34.8%)	
Creatinine Clearance by CKD-EPI equation Ḿ ±SD (range) ,ml/min/1.37m^2	72.2 ±20.9 (34-122)	55.9 ±14.6 (31-94)	**0.003**
Urinary albumin creatinine ratio Median (range) , mg/g	33 (3-1100)	30.5 (11-6700)	**0.04**

Results & Discussion

Comparison between diabetic donors on metformin alone versus metformin combination with other oral hypoglycemic agents.

	Diabetic donors on metformin alone	Diabetic donors on metformin combination	P Value
Frequency, (%)	17/43 (39.5%)	8/43 (18.6%)	
Creatinine Clearance by CKD-EPI equation Ḿ ±SD(range) ,ml/min/1.37m^2	82.8 ±17 (65-122)	49.8 ±2.7 (43-51)	**< 0.0001**
Urinary albumin creatinine Ratio Median (range) , mg/g	25 (3-50)	345 (55-1100)	**0.009**
Fasting blood glucose Ḿ ±SD(range) ,mg/dl	133.2 ± 44.3 (82-166)	145 ± 59.4 (93-198)	0.081

Conclusion & Recommendations

Conclusion

- The incidence of post-donation DM in this study was lower than the general Egyptian population. However, the incidence of micro-macroalbuminuria and/or decreased creatinine clearance was significantly higher than other studies.

- The impact of family history of DM was found highly significant especially on the development of diabetic nephropathy.

- Also there was a positive correlation between the albumin creatinine ratio and post-donation BMI.

- Diabetic donors on RAS blockade, Metformin and insulin showed improvement in albumin creatinine ratio levels and or estimated creatinine clearance. However, donors on other oral hypoglycemic agents, metformin combination with sulfonylureas and other types of antihypertensive medications showed deterioration of albumin creatinine ratio and or creatinine clearance.

RECOMMENDATIONS

- **As regard the study:-**
  - Multiple transplant centers should collaborate in a larger randomized control trial researching live kidney donation related morbidities.

- **As regard donor follow ups:-**
  - Meticulous post-live kidney donation follow ups may improve the outcome of the transplant process and increase the donor pool.

RECOMMENDATIONS

- **As regard donor selection protocols.**
  - We must consider reducing the cutoff point of BMI exclusion, and most importantly to strongly advice donors not to gain Weight after donation giving the positive correlation between BMI and urinary albumin creatinine ratio post-donation.
  - We must also consider exclusion of donors with two or more members of the first degree relatives with a history of diabetes mellitus giving the impact of the family history of diabetes on both development of diabetes and diabetic nephropathy in particular. High risk consent should be obtained if the previously described donors still highly motivated to continue the preparation process.
  - Donors with impaired fasting and/or impaired glucose tolerance should be excluded from the preparation program.
  - Donors with hyperlipidemia should be considered marginal donors. Giving the positive correlation between the serum total cholesterol levels and the urinary albumin creatinine ratio.

RECOMMENDATIONS

- **As regard post-donation follow up policy.**
  - Fasting and two hour post prandial blood glucose levels should be performed as frequent as possible for early diagnosis of diabetes or prediabetes.
  - We must consider albuminuria preventive measures in both pre-diabetics and diabetics. For example, we should consider starting a small dose of RAS blockade even in normotensive diabetic and pre-diabetic donors.
  - We should strongly advise obese donors to start modifying their lifestyles aiming to reduce their weights giving the positive correlation between both the BMI and urinary albumin creatinine ratio.
  - We should have a lower threshold of starting metformin giving its proven beneficial effects on both urinary albumin creatinine ratio and creatinine clearance.
  - On failure of metformin to achieve the desired glycemic control we should add insulin giving its proven beneficial effects on both urinary albumin creatinine ratio and creatinine clearance.
  - We should consider avoiding metformin combination with sulfonylureas as this combination caused deterioration in both renal function and urinary albumin excretion in the studied diabetic donors.
  - Antihyperlipidemic agents should be started as early as possible giving the positive correlation between the serum total cholesterol levels and urinary albumin creatinine ratio.

Thank you